Proceedings of the Iowa Academy of Science

Volume 73 | Annual Issue Article 43

1966

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Herbert K. Brunkhorst
Coe College

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HERBERT K. BRUNKHORST

Abstract: Treatment of white rats with 0.1% methimazole (Tapazole), in distilled water brought about characteristic effects of antithyroid drugs on food intake, body weight, and organ weights, but, did not cause any apparent change in water balance and choride intake and output.

White rats rendered hypothyroid by surgical thyroidectomy showed a decreased water intake as compared to controls (Fregly *et al*, 1960). Treatment with the antithyroid drugs, propylthiouracil, thiouracil, and methimazole (Tapazole), brought about increased water intakes and urinary outputs when given at the dietary level of 0.1% in Purina laboratory meal. (Fregly, 1961). The purpose of the present study was to determine the effect of the most potent of these drugs, methimazole (Stanley and Astwood, 1963), on fluid intakes and urinary outputs when given in the sole source of fluid. A further purpose was to ascertain whether methimazole administered in water affected organ weights of rats in the same way as food containing the same per cent composition of the drug. Still a further objective was to compare urinary chloride outputs of treated rats with those of controls, and, if possible, to ascertain the degree of balance between chloride intake and chloride output in the experimental and control animals.

METHODS

Eleven male rats of Holtzman strain and 58-63 days old were used at the start of the experiment. The animals were housed in individual round metabolism cages in a temperature controlled room maintained at 25 ± 2°C. The animals were weighed daily with a triple-beam animal balance. Food was placed in metal spill-proof containers and fluid in drinking bottles with metal screw caps. Food and water intakes were measured daily by means of the weight displacement method. Pyrex plates covered with copper screening and filled to a depth of a ¼ inch with paraffin oil to prevent evaporation were placed beneath the cages. Urine volumes were measured daily at approximately 11:00 A.M. by placing the combined urine and paraffin oil into separatory funnels and drawing off the urine into graduate cylinders. Urinary chloride determinations were made by a method outlined by Armstrong, (1965).

All animals were placed on distilled water for five days for purposes of becoming accustomed to their surroundings. On

[1] Biology Department, Coe College, Cedar Rapids, Iowa

the sixth day, six of the animals were placed on 0.1% Tapazole[2] dissolved in distilled water. All animals were fed Purina ground laboratory meal throughout the experiment which lasted 18 days.

At the conclusion of the experiment the animals were sacrificed by chloroform inhalation, weighed, and selected body organs removed. The organs were carefully stripped of fat and other tissue, placed in petri dishes containing slightly moistened filter paper, and weighed with a Roller-Smith torsion balance. The organs were then placed into a drying oven and weighed periodically until a constant weight was attained. Organ weight to body weight ratios were calculated and the water content of each organ determined.

Results

At the end of the five day acclimation period, the control animals weighed an average of 271.6 grams, while the experimental animals weighed 273.4 grams. During the next 18 days the control animals steadily increased in weight whereas the tapazole treated animals lost weight. The food intake was 6.7 grams/100 grams of body weight/day for the controls and 5.0 for the experimental group for the 18 day period. The fluid intakes averaged 14.4 ml./100 gm. body weight/day for the controls and 10.0 for the experimental group. Urinary volume outputs in ml./100 gm. body weight/day were lower for the experimental rats, 8.5, as compared to 12.3 for the control animals. Therefore tapazole in water causes less fluid ingestion and urinary output. However, that the ratio of urinary output to fluid intake was very nearly the same for both groups; .847 for the control animals and .850 for the experimental animals, suggests

Table 1. Summary of Daily Measurements

Animals	No. of Rats	Mean Body Weight at beginning of expt. (Gm.)	Mean Body Weight end of expt. (18 days later) (Gm.)	% Increase or Decrease
Controls	5	271.6	340.9	+20.4
Tapazole-treated	6	273.4	260.6	— 4.7

		Food Intake (gm./100 gm. B. W./day)	Fluid Intake (ml./100 gm. B. W./day)	Urinary Volume Output (ml./100 gm. B. W./day
Controls	5	6.7	14.4	12.3
Tapazole-treated	6	5.0	10.0	8.5

		Urinary Output / Fluid Intake	Ratios
Controls	5	.847	
Tapazole-	6	.850	

[2] Courtesy of Dr. Glenn Irving, Eli Lilly Co., Indianapolis, Indiana

that the weight loss of the tapazole animals was not a result of a water imbalance favoring dehydration, but because of lowered food intake. This data is all contained in Table 1.

The organ weight/body weight ratios of the experiment are shown in Table 2a. The thyroid, adrenal, and tests are larger per 100 grams of body weight with tapazole treatment, whereas the thymus, heart, and kidney weights are lower. These results are characteristic of antithyroid treatment, (Fregly and Hood (1959), (Fregly and Cook (1960). That the relative enlargement and decrease in size involves tissue development and is not due to water differences is shown in Table 2b.

Table 2a. Effect of Tapazole on the Organ Weight to Body Weight Ratio of Certain Organs.

Animals	No. of Rates	Initial Mean Body Weight (Gm.)	Final Mean Body Weight (Gm.)	(mg./100 gm.) Weight Ratio Organ Weight/Body		
				Adrenal	Thyroid	Testes
Control	5	282.7	346.7	9.2	6.1	911.0
Tapazole-treated	6	283.3	255.6	16.6	24.7	1064.0
				Thymus	Heart	Kidney
Control				116.9	306.8	942.4
Tapazole-treated				88.7	277.5	931.3

Table 2b. Effect of Tapazole on the Water Content of Certain Organs.

Animals	No. of Rats	Water (%)					
		Adrenal	Thyroid	Testes	Thymus	Heart	Kidney
Control	5	74.9	82.3	87.3	78.1	76.4	77.1
Tapazole-treated	6	70.2	82.1	85.1	79.7	76.1	77.5

The average total mEq. of chloride intake per rat per day, and the average total of urinary chloride output per day expressed as mEq. of chloride contained in sodium chloride are shown in Table 3, for the 18 day experimental period.

Table 3. Effect of Tapazole on Chloride Intake and Output.

Animals	No. of Rats	Intake of chloride expressed in mEq. Cl–/day[3]	Urinary choride output expressed as mEq. Cl– in NaCl/day	Urinary volumes ml./100 gm. B. W./day
Control	5	3.08	2.49	12.3
Tapazole-treated	6	2.01	1.66	8.5
Ratio-Tap./Control		.652	.665	.690
		Ratio of Chloride output/Chloride input		
Control			.811	
Tapazole-treated			.828	

[3] .146 mEq. chloride/kg. by analysis data from Purina Co.

Although there is a decrease in chloride intake by the experimental animals it is, of course, in ratio to the lowered food intake. Total urinary chloride output per day in the experimental animals also decreased but was consistent with the urinary output decrease per day of the experimental group as shown by the similarity of the ratios in the table. Of interest is the ratio between the numerical value of the intake and outputs of the control and experimental animals. It is .811 in the control and .828 in the experimental which would seem to indicate that salt balance had not been disturbed by tapazole treatment.

Discussion

The hypothyroid and goitrogenic effects of tapazole were asserted in this experiment as indicated by the lowered food intake, lack of growth, and typical effects on organs (Fregly and Hood, 1959), (Fregly and Cook, 1960). Despite these effects the water balance of the experimental animals was not affected as indicated by the almost identical ratios of urinary output to water intake, see Table 1. The 15% of water not accounted for was in all probability lost through the lungs and feces. Also, probably some urine was trapped on the mesh screen placed beneath the metabolism cages, and within the food particles which filtered through the screen.

The increased water intake and urinary output in rats treated with 0.1% tapazole in food was not evidenced in this study as it had been by Fregly and his associates. Indeed just the reverse occurred. It is thought that the taste of tapazole cut down on fluid intake, therefore a decrease in urinary output. Unfortunately the laboratory equipment available did not permit sodium analysis of urine, but ratios of chloride output and chloride intake indicated no differences between the experimental and the control animals. One may therefore speculate that the sodium as well as the chloride balance was not affected in this study. This is in agreement with (Fregly *et al*, 1962) in that 0.1% propylthiouracil in food did not affect the sodium and chloride balance of rats unless the rats were placed under some type of stress such as a period of sodium deficiency. In the present study both experimental and control animals always had an adequate sodium chloride diet. Under conditions of sodium deprivation the renal tubules do not reabsorb sodium because of a decreased influence of aldosterone on the tubule's sodium reabsorptive power (Taylor and Fregly, 1964). These authors are of the opinion that renal tubule cells loose their reabsorptive power under the influence of antithyroid drugs. Other interesting experimtal work has shown that there is a lowered secretion of

aldosterone when animals are fed 0.1% propylthiouracil (Fregly *et al,* 1965).

ACKNOWLEDGEMENTS

I thank Dr. Ruth Siemer and Dr. Kenneth M. Cook for their criticism of the manuscript, and their valuable technical assistance.

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Electroencephalograms of Kittens Exhibiting Spastic Behavior

KENNETH M. COOK[1]
WADE L. COLLIER[2]

Abstract. Examination and comparison of some basic reflex tests and of the electroencephalograms of five kittens showing spastic behavior with a control permitted the grouping of these animals into categories which were in accord with those previously determined on the basis of behavioral observation only.

Observations made of a litter of kittens showed varying degrees of lack of coordination in feeding and general behavior. It was decided to extend the scope of the observations by subjecting the animals to an established general static reflex test, a righting test, and a pupil constriction test as well as by the recording of electroencephalograms.

METHODS

Five spastic[3] six-week old kittens from the same litter and one

[1] Associate Professor of Biology, Coe College, Cedar Rapids, Iowa.
[2] Student, Department ofBiology, Coe College, Cedar Rapids, Iowa.
[3] Spastic is defined here in a general sense denoting uncoordinated and at times jerky behavior.